Annex 1: European Collaboration on Craniofacial Anomalies (EUROCRAN)

Background

In 2000 a partnership of 14 European centres was awarded funding under the European Commission's Framework V Programme for research to carry out the EUROCRAN project. EUROCRAN, which will run for four years – between 2000 and 2004 – brings together researchers from a range of clinical/scientific disciplines with the shared aim of improving the management and understanding of craniofacial anomalies (CFA). This will be achieved through five inter-related work packages *(see Annex 2)*.

Participation

The work described in the work packages will be achieved through the development of common core protocols and with the involvement of participating centres from the European Union, the European Economic Area and the states of Central and Eastern Europe.

If you would like to participate or require more information please contact:

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Further materials compiled by EUROCRAN is included as follows:

Annex 2: Work packages
Annex 3: Policy statements
Annex 4: Practice guidelines
Annex 5: General principles governing record-taking (provisional)

Annex 2: Work packages

Work package 1: Surgical trial

A multi-centre randomized trial of the primary surgery for infants with complete unilateral cleft lip and palate will compare four surgical methods in three concurrent trials. Infants will be randomized to a surgical method common to all three trials or the usual local method. Surgeons will do an approximately equal number of their usual method and the common method according to the randomization scheme maintained at the trial coordinating centre.

Work package 2: Gene/environment study

A population-based multi-centre case-parent triad study to investigate gene/environment, and gene/gene interactions and genetic susceptibility polymorphisms operating in the etiology of orofacial clefting (OFC) will be carried out. Mothers with affected babies who are participating in the study will complete a structured interview regarding diet and other exposures in the periconceptual period. In addition samples will be taken from the mother, father and child for DNA extraction and genotyping. Gene variant analysis will then be carried out to investigate the interaction between:

(a) maternal nutritional factors and maternal/fetal metabolism genes;

(b) genes coding for xenobiotic metabolism enzymes and environmental teratogens;

(c) developmental genes (growth factor genes, homeobox genes) and environmental factors.

Work package 3: A chromosomal approach to identifying OFC genes

A cohort of European patients with OFC associated with apparently balanced chromosomal rearrangements will be identified and their breakpoints/clinical phenotypes catalogued. A bank of immortalized cell lines will be established from a sub-set of these patients where two or more instances of a specific breakpoint has been associated with OFC. Both high throughput molecular cytogenetic techniques and available sequence data from the Human Genome Project will be used to identify genes that have been interrupted by two or more breakpoints. These genes will be fully characterized and screened for mutations and polymorphisms that may be used in Work Package 2.

Work package 4: Molecular diagnosis of monogenic craniofacial anomalies

The aim is to develop sensitive molecular assays for the mutations underlying a number of craniofacial malformation syndromes using Treacher Collins Syndrome (TCS) as a paradigm. This expertise will be disseminated to other molecular laboratories in the EUROCRAN group such that it will be available on a local basis.

Work package 5: Directory of resources

A European Craniofacial Anomalies Directory of resources for European teams will be created. The Directory will include:

- a register of clinical teams, their reported clinical protocols and research interests, governmental and non-governmental agencies involved in the treatment and research of CFA, European CFA surgical missions to developing countries, model research protocols and examples of successful grant applications;
- a dynamic database/website of emerging data from Work Packages 2 and 3 such as chromosomal breakpoints, candidate genes and study protocols;
- a "good practice" set of clinical records for consecutive cases of OFC including cephalometric radiographs, dental casts, photographs and speech samples so that teams can compare local outcomes to the reference set;
- a prospective registry of complex treatment outcomes using distraction osteogenesis as an exemplar.

Annex 3: Policy statements

(1) The professional involved in cleft care should provide basic information on cleft care and on the proposed treatment to any potential patient and/or patient's guardian. Basic information should contain at least:

- a general explanation of the condition, the reasons for treatment, what may or may not be achieved, the stages of treatment including examination, record collection and general protocols – this may be supplemented by leaflets, booklets or other kinds of information;
- an explanation of why a specific treatment is considered necessary for the individual patient, what specifically is involved: method, timing, duration cost, what the specific goal is and possible side effects.

(2) When a treatment is considered, the professional engaged in cleft care should take into consideration the desires and attitudes of the patient and/or those of the patient's guardian. The professional should also pay attention to and inform the patient/patient's guardian of the risks and benefits inherent in the potential alternative treatment options, including no treatment or no further treatment.

(3) If requested, it is the professional's responsibility to provide a procedure for obtaining a second opinion for the patient. If requested, this procedure should be communicated to the patient before treatment starts.

(4) After an episode of treatment, the professional engaged in cleft care should inform the patient and/or patient's guardian on:

- outcome of treatment relative to the defined goal;
- undesirable effects of treatment;
- expected future development.

(5) The professional engaged in cleft care should analyse and document any complaints or praise expressed by the patient and/or the patient's guardian.

(6) The professional engaged in cleft care should give consideration to the burden of the treatment. Considerations should include financial as well as non-financial burden, such as treatment duration, effort from the patient and/or patient's guardian and discomfort as a result of treatment.

(7) During the process of treatment, the professional involved in cleft care should continuously evaluate treatment progress against the planned treatment and act accordingly.

(8) Organizations and institutes responsible for the provision of cleft care should:

- encourage the cleft professional to follow the policies described above and to acknowledge the patient's rights;
- recognize and encourage the professional's right to provide treatment that can be expected to improve the patient's condition whilst minimizing adverse effects;
- recognize and encourage that decisions on treatment priority should be based on criteria proposed by the cleft professionals in consultation with the patient and/or patient's guardian. This is especially so in a situation with insufficient treatment resources;
- recognize and encourage that access to treatment should not depend on the patient's ability to pay;
- recognize that cooperation of the patient with the advice and instructions of the cleft professional is necessary in order to achieve a successful result.

Annex 4: Practice guidelines

Part I: Health-care needs

(1) **Neonatal emotional support and professional advice:** In the event of prenatal diagnosis and as soon as possible after the birth of a child with a cleft, parents should be given emotional support and advice about the child's future management by a specialist in cleft care.

(2) **Neonatal nursing:** Difficulties in feeding are common in the early days of life and specialist advice on feeding should be provided.

(3) **Surgery:** Primary surgery to close clefts of the lip and/or palate should be performed by an experienced and qualified surgeon according to a protocol agreed by the team. Further corrective procedures may be necessary for some patients in later years and should be performed by an experienced and qualified surgeon according to a protocol agreed by the team.

(4) **Orthodontic/orthopaedic treatment:** For children with cleft lip and palate orthodontic/orthopaedic treatment should be available when necessary and should be performed by an experienced orthodontist.

(5) **Speech and language therapy:** Early assessment of speech and language problems, advice to parents and the availability of corrective therapy by an experienced speech and language therapist should be provided.

(6) **Ear, nose and throat (ENT):** ENT problems should be identified at an early stage and the necessary therapy should be provided.

(7) **Clinical genetics/paediatric developmental medicine:** As cleft lip and/or palate may be associated with other anomalies early assessment and diagnosis is necessary. Genetic counselling for patients and families should be available.

(8) **Emotional support and professional advice for the growing child and its parents:** Emotional support and professional advice for parents, patients and their environment is often necessary and should be available.

(9) **Dental care:** Regular dental care should be available.

(10) **National register:** A national register should be in place for accurate recording of children born with cleft lip and/or palate and related craniofacial anomalies.

Part II: Organization of services

(1) Cleft care should be provided by a multidisciplinary team of specialists.

(2) Members of the team should have special training in cleft care.

(3) The team should agree on the stages of treatment including the examination, record collection and general protocols.

(4) There should be one person responsible for quality improvement and communication within the team.

(5) Coordination of the care of individual patients is important since numerous specialities are involved. This should be the responsibility of one member of the team.

(6) The number of patients referred to the team should be sufficient to sustain the experience and specialist skills of all team members and to allow evaluation/audit of the team's performance within a reasonable period of time. It has been recommended that cleft surgeons, orthodontists and speech therapists should treat at least 40-50 new cases annually. However, it is recognized that individual member states have the right to provide care for their own population.

Part III: Finances

Resources should be available to cover the following care for children with cleft lip and palate:

(1) Emotional support and professional advice during the neonatal period.

(2) Neonatal nursing.

(3) Surgery.

(4) Orthodontic/orthopaedic treatment.

(5) Speech and language assessment and therapy.

(6) Ear, nose and throat treatment.

(7) Clinical genetics/paediatric developmental medicine.

(8) Emotional support for the growing child and its parents.

(9) Travel expenses.

(10) General dental care including cleft related prosthodontics.

Annex 5: General principles governing record-taking (provisional)

1. Records for treatment planning/monitoring

- Clinical records should be taken for individual patients to allow treatment planning, monitoring treatment progress and treatment evaluation.
- The timing and nature of these records will depend on the clinical protocols followed by individual teams.
- Treatment and associated record-taking protocols should be agreed and clearly set out by the cleft team.

2. Records for quality improvement/research

Additional records may be taken for a number of other reasons:

- follow-up of a series of patients to provide an overview of the outcome of care;
- to allow retrospective comparisons of different protocols;
- as part of a prospective clinical trial with ethical approval;
- as part of an agreed protocol for intercentre quality-improvement comparisons or comparison against known standards;
- as part of an agreed research protocol;
- other reasons, such as medico-legal, second opinion.

3. Safeguards

- Exposure of patients to unnecessary radiation should be avoided.
- Research and quality-improvement records should only be taken when there is an established written protocol on how they will be put to use.
- Research and quality improvement records should not be taken without the consent of the patient/parent/guardian.
- Research and quality improvement records should coincide as far as possible with the records for treatment planning/monitoring (statement 1 above).

4. Timing of minimum records

Table 1: Complete cleft lip and palate (UCLP & BCLP)

Timing	Models	Lateral skull radiograph	Photographs	Speech/ tympanometry	Audiometry	Patient/parent satisfaction
Primary surgery	✓		✓			
3 years				✓*	✓*	
5/6 years	✓		✓	✓	✓	
10 years	✓	✓	✓	✓	✓	
18+ years	✓	✓	✓	✓		✓

* = If hard palate is closed.

Table 2: Cleft palate only

Timing	Models	Lateral skull radiograph	Photographs	Speech/ tympanometry	Audiometry	Patient/parent satisfaction
Primary surgery	✓		✓			
3 years				✓	✓	
5/6 years	✓			✓	✓	
15/16 years	✓	✓	✓	✓	✓	✓

Table 3: Cleft lip only

Timing	Models	Photographs	Patient/ parent satisfaction
Primary surgery	✓*	✓	
3 years			
5/6 years	✓*	✓	
10 years			
18+ years		✓	✓

* = Only in cases with cleft of the alveolus as well as cleft lip.

Table 4: Alveolar bone grafting

Timing	Intra-oral x-ray	Photographs
Just before bone graft	✓	✓
6 months after graft	✓	
After canine fully erupted	✓	✓

Table 5: Pharyngoplasty

Timing	Speech sample
Just before operation	✓
One year after operation	✓

Table 6: Orthognathic surgery

Timing	Lateral cephalogram	Models
Just before operation	✓	✓
One year after operation	✓	✓

5. Record-taking methodology (provisional)

Discussion of the precise method of record taking is continuing. The following however, provide a suggestion that is currently being used widely in Europe.

5.1 Photographs

Background: The vast majority of surgeons and orthodontists use still photographs for documentation of clefts. Very few clinicians use video recording of clefts pre- or post-operatively. If photographs of clefts which appear in any publication are examined it is clear that there is no uniformity or standardization of the way in which such photographs are taken. For comparative studies the following views are recommended.

Basic views to be taken:

- Frontal, both laterals, inferior (columellar) view.
- Three-quarter (¾) facial (oblique) view.

Dynamic views:

- During smiling and whistling – in the cooperative older patient, these views will give an idea of function of the circum-oral musculature.
- Video recording will be better for assessing circum-oral movement but this will also need to be standardized and cannot be used routinely at present.

Lighting and background:

- Lighting for the studio should be two fill-in lights and the main light synchronized with the camera. In the ward or operating theatre a single flash unit is appropriate.
- The background should be blue.

Framing of the picture:

- For frontal view, the camera should be set at a ratio of 1:8.
- For lateral view, the camera should be set at a ratio of 1:8.
- For inferior view, the camera should be set at a ratio of 1:4.

Camera and lens:

- Suggested camera is Nikon F3 with a 105mm lens or equivalent.
- Film type and speed need not be standardized.

5.2 Dental casts

Background: Dental casts need to be made from well-taken impressions which include all teeth, the palate and the buccal sulcus. For comparative studies the casts need to be prepared in a standard manner so that the source of the models cannot be identified.

Preparation: Models should be:

- cast in vacuum-mixed white stone, for example Crystacal R;
- hand trimmed, using a fine wheel to the standard heights and angles shown in Figures 1-3 below;
- finished with wet and dry paper (not soaped).

Figure 1:
Base angles of a dental cast

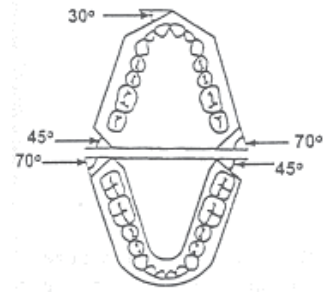


Figure 2:
Dental casts of a 10-year old

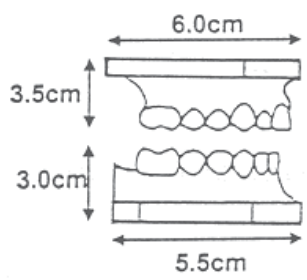
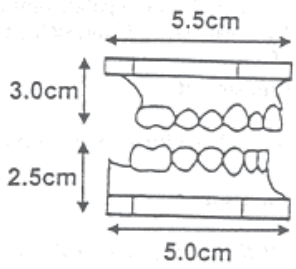


Figure 3:
Dental casts of a 5-year old



5.3 Speech

Background: A fundamental problem for speech and language pathology has been the lack of an acceptable framework for measuring speech. Various groups have proposed procedures for measuring, recording and reporting speech data cross-linguistically, but to date there is no one recognized method.

Proposals have come from Henningsson and Hutters (1997), and also from Dalston, Marsh, Vig, Witzel and Bumstead (1988). In Britain, Sell, Harding and Grunwell (1994) developed the Great Ormond Street speech assessment (GOS.SP.ASS) tool. This is now a nationally-agreed speech

assessment tool for cleft palate and/or velopharyngeal incompetence in English. From GOS.SP.ASS, Razzell, Harding and Harland (1987) devised the Cleft Audit Protocol for Speech (CAPS), a more succinct protocol specifically designed for audit purposes.

Ages: 3-4 years; 5-6 years; 10 years; 15-16 years (cleft palate only); 18+ years (UCLP and BCLP)

Equipment: A good quality audio recording using a high quality microphone.

Variables:

- **Intelligibility**: a rating should be made upon spontaneous speech. The CAPS scale can be used to judge how "understandable" a persons speech would be to familiar and unfamiliar listeners (there are however flaws with this method).
- **Nasality**: the presence/absence and degree of hypernasality, hyponasality, audible nasal emission and nasal turbulence can be judged and rated on a five-point scale (see CAPS). An agreed instrumental method for assessing nasality has yet to be recommended.
- **Assessing articulation**: set sentences and single words containing consonant sounds in different word positions (beginning, middle and end) should be repeated, for example "Bob is a baby boy" or equivalent in the native language, and recorded for CAPS. Targeted sounds are*: p, b, f, n, t, d, s, ʃ, ʧ, ʤ, k, g.

  Errors made can be broadly categorized or grouped according to CAPS:
  - front of mouth oral-sound errors;
  - back of mouth oral-sound errors;
  - non-oral sounds;
  - passive errors;
  - immaturities.

References:

- Henningsson G, Hutters B. Perceptual assessment of cleft palate speech with special reference to minimum standards for intercentre comparisons of speech outcome. In: Lee ST, Huang M, eds. *Transactions 8th International Congress on Cleft Palate and Related Craniofacial Anomalies.* Stamford Press Pte Ltd: Singapore 1997.
- Dalston M, Marsh JL, Vig KW, Witzel MA, Bumstead RM. Minimal standards for reporting the results of surgery on patients with cleft lip, cleft palate, or both: A Proposal. *Cleft Palate Journal,* 1988; 25: 3-7.
- Sell D, Harding A, Grunwell P A. Screening assessment of cleft palate speech (Great Ormond Street speech assessment: GOS.SP.ASS). *European Journal of Disorders of Communication,* 1994; 29: 1-15.
- Harding A, Harland K, Razzell R. *Cleft Audit Protocol for Speech (CAPS).* Available from K Harland, Speech and Language Therapy Department, St. Andrew's Plastic Surgery Centre, Stock Road, Billericay, Essex CM12 OBH, United Kingdom, 1987.

* Depending on the speech sound in each language, but should contain plosives, fricatives and a nasal consonant (p, b, t, d, k, g, f, s, n).